CADTH

CADTH DRUG REIMBURSEMENT REVIEW

Pharmacoeconomic Report

ATEZOLIZUMAB (TECENTRIQ) + BEVACIZUMAB

(Hoffmann-La Roche Limited)

Indication: in combination with platinum-based chemotherapy for the treatment of locally advanced or metastatic non-squamous non-small cell lung cancer in patients with EGFR or ALK genomic tumour aberrations who have progress on treatment with targeted therapies.

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About CADTH: CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.

Funding: CADTH receives funding from Canada's federal, provincial, and territorial governments, with the exception of Quebec.

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Abbreviations

ABCP	atezolizumab bevacizumab carboplatin paclitaxel
ALK	anaplastic lymphoma kinase
BIA	budget impact analysis
CGP	clinical guidance panel
EGFR	epidermal growth factor receptor
ICER	incremental cost-effectiveness ratio
kg	kilogram
KM	Kaplan-Meier
LY	life-year
mg	milligram
mL	milliliter
NOC	notice of compliance
NSCLC	non-small cell lung cancer
OS	overall survival
PFS	progression-free survival
PSM	partitioned survival model
QALY	quality-adjusted life-year

Executive Summary

The executive summary is comprised of two tables: Table 1 Background and Table 2: Economic Evaluation) and a conclusion.

Table 1: Submitted for Review

Item	Description
Drug product	Atezolizumab (Tecentriq), 1200 mg vial for intravenous infusion and bevacizumab, 100 mg or 400 mg vials for intravenous infusion.
Submitted price	Atezolizumab, 1200 mg / 20 mL, intravenous infusion: $6,776.00 per vial Bevacizumab, 100 mg / 4 mL, intravenous infusion: $519.18 per vial Bevacizumab, 400 mg / 16 mL, intravenous infusion: $2,076.71 per vial
Indication	Atezolizumab in combination with bevacizumab, paclitaxel and carboplatin for the first-line treatment of adult patients with metastatic non-squamous NSCLC, with no EGFR or ALK genomic tumour aberrations, and no prior systemic chemotherapy treatment for metastatic non-squamous NSCLC.
Health Canada approval status	NOC
Health Canada review pathway	Standard review
NOC date	May 24, 2019
Reimbursement request	Atezolizumab in combination with bevacizumab and a platinum-based chemotherapy for the treatment of metastatic EGFR and/or ALK positive non-squamous non-small cell lung cancer patients who have progressed on treatment with targeted therapies. Maintenance atezolizumab should be continued until loss of clinical benefit or unacceptable toxicity. Maintenance bevacizumab should be continued until disease progression or unacceptable toxicity.
Sponsor	Hoffmann-La Roche Limited
Submission history	Previously reviewed: No

mg = Milligram; mL = Milliliter; NOC = Notice of Compliance;

Table 2: Summary of Economic Evaluation

Component	Description
Type of economic evaluation	Cost-utility analysis, cost-effectiveness analysis Partitioned survival model
Target population	Patients with locally advanced or metastatic non-squamous NSCLC with EGFR- and/or ALK genomic tumour aberrations (i.e., EGFR or ALK+) who have progressed on treatment with targeted therapies
Treatment	Atezolizumab and bevacizumab in combination with carboplatin and paclitaxel followed by atezolizumab and bevacizumab maintenance
Comparator	Platinum-based chemotherapy in combination with pemetrexed followed by pemetrexed maintenance
Perspective	Canadian publicly funded health care payer
Outcomes	QALYs, LYs
Time horizon	Lifetime (ten years)
Key data source	IMpower150 trial for atezolizumab and bevacizumab treatment efficacy; network meta-analysis (NMA) for comparator treatment efficacy
Submitted results for base case	ICER = $362,346 per QALY (0.66 QALY, $239,629 incremental costs)
Key limitations	• Uncertainty exists as to the comparative efficacy of ABCP and platinum-based chemotherapy plus pemetrexed. The NMA used data from populations that may not be comparable and excluded key comparators and trials. As a result, the magnitude of clinical benefit with ABCP is highly uncertain. • Several issues were identified with the implementation and extrapolation of the clinical data within the submitted economic evaluation, which included median OS not being reached in the observed period, a long plateau in the OS curve being informed by fewer than 10 participants and the OS and PFS curves crossing. This led to uncertainty with the approximation and extrapolation of the observed data within the model, particularly given much of the benefit observed with ABCP was over the extrapolation period. • A proximity-to-death approach was used to describe patient health states, which is not aligned with the event leading to the largest change in patient utility (i.e., being on or off treatment), nor has this approach been well validated. Additionally, the sponsor excluded adverse event disutilities, the impact of which would not be captured in routine utility questionnaires. • The proportion of patients on each initial therapy receiving subsequent therapy following discontinuation, as well as the distribution of subsequent therapies, was not representative of the Canadian setting, likely overestimating the costs for patients on platinum-based chemotherapy plus pemetrexed. • Biosimilar bevacizumab is less costly than the sponsor submitted price for branded bevacizumab, likely overestimating costs associated with ABCP. Clinical expert feedback indicated biosimilar bevacizumab was likely to be used in clinical practice instead of the branded option.
CADTH reanalysis results	• CADTH conducted a reanalysis which included: applying utilities based on patients being on or off treatment, incorporating disutilities for treatment-related adverse events, updating the proportion of patients on subsequent therapy and the distributions of those therapies to be more representative of Canadian clinical practice, and use of the biosimilar price for bevacizumab. Issues related to the comparative efficacy of ABCP could not be addressed, while issues related to the implementation and extrapolation of clinical data were assessed in scenario analyses. • Based on CADTH reanalyses, the ICER = $430,339 per QALY • At a price reduction of 99% for atezolizumab, the ICER is $158,883 per QALY gained. It is highly unlikely that ABCP would be considered cost-effective at conventionally accepted ICER thresholds ($50,000 or $100,000 per QALY), unless there were significant price reductions for both atezolizumab and bevacizumab.

ALK = anaplastic lymphoma kinase; EGFR = epidermal growth factor receptor; ICER = incremental cost-effectiveness ratio; LY = life-year; NMA = network meta-analysis; NSCLC = non-small cell lung cancer; PSM = partitioned survival model; QALY= quality-adjusted life-year

Conclusions

CADTH undertook reanalyses of the sponsor's economic submission to address some of the identified limitations: applying utilities based on patients being on or off treatment, incorporating disutilities for treatment-related adverse events, updating the proportion of patients on subsequent therapy and the distributions of those therapies to be more representative of Canadian clinical practice, and use of the biosimilar price for bevacizumab. Based on CADTH reanalyses, the ICER for ABCP compared to platinum-based chemotherapy plus pemetrexed was $430,339 per QALY gained. The results are primarily driven by the combined cost of treatment for bevacizumab and atezolizumab. Even at a 99% price reduction for atezolizumab, the ICER remains over even a $100,000 per QALY, as the cost of bevacizumab remains high. Along with a 99% price reduction for atezolizumab, the price of biosimilar bevacizumab would need to be approximately 46% below current list price for the ICER to fall below $100,000 per QALY or approximately 85% to fall below $50,000 per QALY.

The comparative clinical evidence used to inform this analysis is highly uncertain as there are concerns regarding the magnitude of effect that has been calculated in this analysis, particularly over the extrapolation period.

Overall it is highly unlikely that ABCP would be considered a cost-effective use of Canadian healthcare resources, at a $50,000 or $100,000 per QALY threshold, even if substantial price reductions were obtained for both atezolizumab and bevacizumab.

Based on the sponsor's submitted budget impact analysis, the total incremental cost is estimated to be [redacted] over the first three years. CADTH reanalyses suggest that the estimated budget impact of introducing ABCP to the market was underestimated, with an estimated incremental cost of $70,005,616 over three years. *(Non-Disclosable information was used in this pCODR Guidance Report and the sponsor requested this economic information not be disclosed pursuant to the pCODR Disclosure of Information Guidelines. This information will remain redacted until notification by the sponsor that it can be publicly disclosed.)*

Stakeholder Input Relevant to the Economic Review

This section outlines the technical details of the pCODR Economic Guidance Panel's evaluation of the economic evidence that is summarized in the executive summary. In accordance with the *Disclosure of Information Guidelines for the CADTH Pan-Canadian Oncology Drug Review*, this section is not eligible for disclosure. It was provided to the pCODR Expert Review Committee (pERC) for their deliberations and the participating drug programs for their information.

Economic Review

This section outlines the technical details of the pCODR Economic Guidance Panel's evaluation of the economic evidence that is summarized in the executive summary. In accordance with the *Disclosure of Information Guidelines for the CADTH Pan-Canadian Oncology Drug Review*, this section is not eligible for disclosure. It was provided to the pCODR Expert Review Committee (pERC) for their deliberations and the participating drug programs for their information.

Appendix 1: Cost Comparison Table

This section outlines the technical details of the pCODR Economic Guidance Panel's evaluation of the economic evidence that is summarized in the executive summary. In accordance with the *Disclosure of Information Guidelines for the CADTH Pan-Canadian Oncology Drug Review*, this section is not eligible for disclosure. It was provided to the pCODR Expert Review Committee (pERC) for their deliberations and the participating drug programs for their information.

Appendix 2: Submission Quality

This section outlines the technical details of the pCODR Economic Guidance Panel's evaluation of the economic evidence that is summarized in the executive summary. In accordance with the *Disclosure of Information Guidelines for the CADTH Pan-Canadian Oncology Drug Review*, this section is not eligible for disclosure. It was provided to the pCODR Expert Review Committee (pERC) for their deliberations and the participating drug programs for their information.

Appendix 3: Additional Information on the Submitted Economic Evaluation

This section outlines the technical details of the pCODR Economic Guidance Panel's evaluation of the economic evidence that is summarized in the executive summary. In accordance with the *Disclosure of Information Guidelines for the CADTH Pan-Canadian Oncology Drug Review*, this section is not eligible for disclosure. It was provided to the pCODR Expert Review Committee (pERC) for their deliberations and the participating drug programs for their information.

Appendix 4: Additional Details on the CADTH Reanalyses and Sensitivity Analyses of the Economic Evaluation

This section outlines the technical details of the pCODR Economic Guidance Panel's evaluation of the economic evidence that is summarized in the executive summary. In accordance with the *Disclosure of Information Guidelines for the CADTH Pan-Canadian Oncology Drug Review*, this section is not eligible for disclosure. It was provided to the pCODR Expert Review Committee (pERC) for their deliberations and the participating drug programs for their information.

Appendix 5: Additional Information on the Submitted BIA

This section outlines the technical details of the pCODR Economic Guidance Panel's evaluation of the economic evidence that is summarized in the executive summary. In accordance with the *Disclosure of Information Guidelines for the CADTH Pan-Canadian Oncology Drug Review*, this section is not eligible for disclosure. It was provided to the pCODR Expert Review Committee (pERC) for their deliberations and the participating drug programs for their information.

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